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Granin - Derived Peptides in the Eye

Editorial

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The granins are the acidic proteins of secretory granules and there exist three main members of this family, in particular chromogranin A, chromogranin B and secretogranin II. These proteins are widely distributed throughout neuroendocrine tissues and are stored in large dense core vesicles in neuronal cells. Their functional role is not fully clear but it seems that they might play an important role in the formation of secretory granules. Furthermore, the primary amino acid sequence of the granins features many pairs of basic amino acids and these pairs together with monobasic residues are targets of enzymes which proteolytically process the proteins, in particular the prohormone convertases 1 and 2. Thus the granins might be precursors of smaller fragments and they are indeed cleaved. Processing of chromogranin A leads to the generation of catestatin, vasostatins, pancreastatin, serpinin, WE-14, chromacin, chromofungin, chromostatin, betagranin and parastatin, of chromogranin B to secretolytin and of secretogranin II to secretoneurin, manserin and EM66. These peptides are either biologically highly active and/or of pathophysiological significance and the peptides with the highest degree of biological activity are secretoneurin, catestatin, vasostatins and pancreastatin. For secretoneurin, outstanding effects have been described, in particular it promotes not only both angiogenesis and vasculogenesis but also therapeutic angiogenesis in the hindlimb ischemia and myocardial infarcation model. Others however seem to be functionally inert, especially the chromogranin A-derived peptide GE-25 and the chromogranin B-derived peptide PE-11.

The eye is the sole sense organ where granin-derived peptides have been explored. The presence and distribution of several granin-derived peptides have been investigated mainly in rats, namely of secretoneurin, PE-11, GE-25, WE-14, catestatin and serpinin and secretoneurin, PE-11, GE-25, catestatin and serpinin are constituents of the sensory innervation of the eye since they are abundantly expressed in the trigeminal ganglion and pretreatment of newborn rats with capsaicin led to a decrease of the levels of secretoneurin and PE-11 in each ocular tissue exept of the retina. Capsaicin predominantly destroys sensory neurons. The other peptides featured colocalization with the typical sensory peptide substance P. The granins seem to become proteolytically processed already at the site of synthesis in the trigeminal ganglion and pronounced processing has also been shown in the retina. In the retina, secretoneurin, WE-14 and catestatin are expressed in cells in the inner retina, predominantly amacrine cells in the proximal inner nuclear layer and displaced amacrine cells in the ganglion cell layer, but PE-11, GE-25 and serpinin in glia. Their functional significance in the eye is completely unknown.

There are certain aims in the research of granin-derived peptides in the eye in the future. On the one hand, the presence and distribution of further granin-derived peptides must be explored in the eye and on the other hand most importantly, to find biological effects of these peptides. Since some of them are biologically highly active, they might be of pathophysiological significance in the eye. For others such as PE-11 or GE-25 no effects have been described so far, an effect would be a completely novel activity. In conclusion, it is important to continue the granin research in the eye and not only in the eye but also in other sense organs, especially in the skin.

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